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Revised Scientific Data Summary Outline

In this version the focus is the story which illustrates why the JLI version of Accord can be considered a PREP. In other words it is an explanation more so than a catalog of the information.


Scientific Data Summary

- ❖ Executive Summary
- ❖ Introduction
- ❖ A PREP Must Meet Product Acceptability Requirements
 - Philip Morris USA Uses a Defined Process for Determining Toxicological Acceptability
 - Description of the guidelines
 - The IOM Report Makes Some Recommendations About Toxicological Acceptability
 - Regulatory Principle #2?
 - Regulatory Principle #7?
- ❖ Evidence Needed to Make a Reduced Exposure Claim
 - Description of Regulatory Principle #4
 - Definitions of reduced exposure, reduced risk and reduced harm
 - This includes a discussion of subjective acceptability in the context of harm
 - Substantial reductions in exposure
 - Anticipated reduction in Morbidity and/or Mortality
 - ~~Harmful substances?~~
- ❖ Philip Morris, USA Evaluation of Reduced Exposure
 - Information about reductions in exposure, which are placed in the context of disease, is required for the evaluation of a cigarette as a PREP?
 - Data on exposure
 - Clinical exposure data which clearly assesses the potential for the product to reduce exposure
 - Human exposure data which provides and assessment of how the product is used
 - Nonclinical data collected under puffing conditions relevant to human smoking
 - Information relative to morbidity/mortality
 - Integration of information into weight of evidence
 - ◆ Description of factors used in the weight of evidence evaluation including levels of evidence
 - ◆ Target Product Profile
 - There is a plan to conduct surveillance and long-term health effects studies
 - This includes an assessment of effects on smoking initiation and cessation

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- Use of ethics committees (animal and human)

For Accord – JLI

- ❖ The Product Evaluated: Electrically Heated Cigarette Smoking System (EHCSS)
 - General description
 - Temperature effects?
 - Use of AMP
 - Subjective targets
- ❖ EHCSS Demonstrates Potential Reductions in Exposure to Harmful Smoke Constituents
 - Human data which assesses exposure (e.g. biomarkers)
 - Short-term study (exposure and use data)
 - The Exposure Reductions for Persons Currently Smoking ~~Menthol~~ Product Are Expected to be Similar to Those Observed for the Regular Version of the Product
 - Human exposure data from short-term menthol study
 - Comparison of the changes in exposure observed in the menthol study with those observed in the study with the regular product
 - Comparison of the smoke chemistry for the menthol and regular versions
 - Conclusion regarding the expected similarity in exposure between the regular and menthol versions
 - Long-term study (exposure and use data)
 - Smoke constituent delivery determined in a manner relevant to human smoking
 - Specific chemicals
 - Ames responsive constituents
 - Cytotoxic constituents
 - Exposure to ETS
 - Other key supporting information
 - Rat lung inflammation
 - 90-day rat inhalation
 - Particle deposition
- ❖  Conclusions: EHCSS is Anticipated to Reduce Morbidity/Mortality of Diseases Associated with Smoking.
 - Cancer
 - Estimated reduction in exposure to carcinogens
 - Smoke chemistry
 - Biomarkers
 - Estimated reduction in exposure to genotoxic compounds
 - Ames assay nonclinical
 - Ames assay on urine
 - Estimated reduction in exposure to cytotoxic compounds as an indicator for promotion?

- COPD
 - Estimated reduction in exposure to aldehydes
 - Estimated reduction in exposure to NOx
 - Estimated reduction in exposure to cytotoxic compounds
 - Reduction in rat lung inflammation
 - CVD
 - Reduction in exposure to CO
 - Reduction in exposure to nicotine ?
 - Positive changes in biomarkers of reduced harm (if available)
 - ETS
 - Commentary related to any disease or adverse health effect associated with exposure to ETS
 - Discussion of any possible increases in exposure
 - Overall Evaluation and Assessment
 - Surveillance Plan
- APPENDIXES

[Note: Some of the statements in this draft are being made in the absence of data solely for the purpose of framing a possible version of this draft. All of those statements are subject to change when the data becomes available and will be changed to reflect an accurate interpretation of the data.]

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